REMARKS

Claims 1-4, 6-14, and 19-24 stand rejected in the Office Action. Claims 1, 8, 9, 11-14 and 22-24 are amended with this Response. Claim 25 has been added. Upon entry of the amendments, claims 1-4, 6-14, and 19-25 are pending.

Three amendments have been made to the specification, to correct typos and formal matters. No new matter is added. Applicant respectfully requests their entry.

Support for the amendments to Claims 1, 8, 9, 11-14 and 22-24 is found in the specification, for example on page 3, line 28, page 4, lines 1-4 and 9-15. The description at pages 2, 4 and 5 has also been amended to correct grammatical errors. The amendments of the description and the claims do not contain new matter. Applicant respectfully requests entry of the amendments.

Request for Personal Interview

Applicant would like to request a personal interview between the Examiner and Applicant's representative prior to examination on the merits. Applicant believes such would help to expedite prosecution. The Examiner is invited to telephone the undersigned if that would be helpful to resolving any issue.

Double Patenting Rejection

Claims 1-4, 6-14, and 19-20 are rejected under the judicially created doctrine of obviousness-type double patenting over Claims 1, 7, 8, and 12 of U.S. Patent 6,117,453 [hereinafter the '453 patent]. Applicant respectfully traverses the rejection as applied to the amended claims and requests reconsideration.

A double patenting rejection of claims over a patent issued to a common assignee is proper if the subject matter of the claims is obvious over the invention claimed in the patent to such an extent that grant of a patent on the new claims would result in an extension of the inventor's monopoly. The key inquiry is whether the subject matter of the rejected claims is

obvious over the claims of the issued patent. For a finding of obviousness to be sustained over a single reference, there must be a motivation elsewhere then in the current application to modify what the reference discloses to arrive at the subject matter of the claims. It is improper to use the current application to provide the motivation.

The amended claims contain a number of limitations not disclosed or suggested in the claims of the '453 patent. Amended claims 1, 9, and 11 recite that the gastroresistant polymer of the coating dissolves in the intestines but not in the stomach and duodenum, and that as the gastroresistant polymer dissolves, verapamil is released in the intestine without influence from food intake. The claims of the '453 patent do not teach or suggest a tablet composition in which verapamil is released without food effect. The claims state merely that a core of a tablet is optionally coated. Further, the claims do not teach or suggest Applicant's specific coating as recited in the rejected claims, that is one containing 30 to 80% of a gastroresistant polymer and 0-30% of polyethylene glycol.

Applicant respectfully submits that there is no motivation to modify the subject matter of Claims 1, 7-8, and 12 of the '453 patent to arrive at the subject matter of amended Claims 1, 9, and 11. The coating of the tablet composition claimed in amended Claims 1, 9 and 11 is not an obvious variation of the coating claimed in Claims 1, 7-8 and 12 of the '453 patent.

Although the '453 patent discloses examples of formulations of actives, other than verapamil, in which the coating contains methacrylic acid copolymers, polyethylene glycol and silicon dioxide, the '453 patent does not suggest or teach a tablet composition of verapamil that is free of food effect as claimed in amended Claims 1, 9 and 11. The tablet composition of verapamil claimed in claims 1, 9 and 11 gives the unexpected result that as the gastroresistant polymer dissolves, verapamil is released in the intestine without influence from food intake. Such a tablet composition is neither disclosed nor suggested by the '453 patent.

Because the subject matter of the amended claims is neither taught nor suggested by the claims of the '453 patent, a rejection for obviousness type double patenting is not proper. Accordingly, Applicant respectfully requests that the rejection be withdrawn.

Applicant notes that Claims 21-24 are not rejected under the double patenting doctrine. Claims 21-24 contain the limitation that the coating is soluble at a pH above 5.5. Thus, the pH 5.5 limitation is a non-obvious variant of the claims of the reference. Applicant respectfully submits that the limitation added to claims 1, 9, and 11 is likewise a non-obvious variant, and further distinguishes the subject matter of the current claims from the claims of the reference. For this additional reason, Applicant respectfully requests that the double patenting rejection be withdrawn.

Rejection Under 35 U.S.C. § 103

Claims 1-4, 6-14, and 19-24 are rejected under § 103 as unpatentable over the Morella reference of record [hereinafter "Morella"]. Applicant respectfully traverses the rejection as applied to the amended claims and requests reconsideration.

To sustain a rejection under § 103 over a single reference, the reference must teach or suggest every element of the claims, and there must be some motivation to modify what the reference discloses to arrive at the subject matter of the claims. Just because a modification can be made, the modification is not obvious unless there is a teaching that such modification would be desirable.

Applicant has amended Claims 1, 9, and 11 to recite that the gastroresistant polymer dissolves in the intestines but not in the stomach and duodenum, and that as the gastroresistant polymer dissolves, verapamil is released in the intestine without influence from food intake. Support for the amendment can be found for example on page 4, lines 1-11.

The Morella reference discloses a pharmaceutical pellet composition comprising a hybrid core coating which must include a polymer that is insoluble regardless of pH, an enteric polymer that is substantially insoluble at acidic pH but at least partially soluble at a less acidic to basic pH, and a polymer that is partially soluble at acidic pH (see column 8, lines 46-51). Morella's coat achieves the desired slow rate of release of the active at acidic pH, and a faster relatively constant rate of release at a less acidic to basic pH. In column 9, at lines 13-16, Morella states

> "the ternary system of polymers according to the present invention allows greater flexibility than as known in prior art using only binary systems of polymers".

Morella designed a ternary system of polymers for the coating so that the active is released throughout the gastrointestinal tract. From column 7, lines 41-44, a skilled person would readily understand that Morella's coating is partially soluble in acidic medium, and as such the release of the active will begin in the stomach. Morella's coating will then continue to dissolve releasing further active even in the region after the pyloric sphincter where it is not sufficiently alkaline to dissolve the enteric polymer (see column 7, lines 46-53). The active will continue to be released in the intestines and there will even be release of the active in the large intestine according to Morella (see column 7, lines 55-58).

In contrast, the tablet composition as claimed in amended Claims 1, 9 and 11 has a polymer component which consists essentially of 0 to 30% by weight of polyethylene glycol and from 30 to 80% of a gastroresistant polymer. The gastroresistant polymer withstands the acidic pH of the stomach and duodenum and will dissolve in the intestines, thereby releasing the active (verapamil) in the intestine. The amended claims further state that release of verapamil occurs without influence from food intake.

A skilled person having read and understood Morella would not be motivated to change its teaching to arrive at the subject matter of the claims, i.e. a coating that has a polymer

component consisting essentially of 0 to 30% by weight of polyethylene glycol and 30 to 80% of a gastroresistant polymer. Based on the discussion below, he would not have expected that the composition of the amended claims would lead to the release of verapamil without food effect.

Although Morella states that the bioavailability of the active is not compromised by food so that the product may be taken without regard to meals (see column 7, lines 36-40), Morella's pharmaceutical pellet composition is not free or devoid of food effect. The ternary polymer system of Morella's coating allows for the release of the active throughout the gastrointestinal tract. In the single dose crossover studies conducted by Morella, it was shown that under fasted conditions, there was no significant difference between the AUC (mean area under the curve) for the Morella formulations (numbered 1 and 2) and the reference (see column 18, lines 54-56). Yet, under fed conditions, the crossover studies, being conducted in the same manner as for the fasted state, showed a significant difference between the AUC for the Morella formulations #1 and #2 and that obtained for the reference (see column 20, lines 52-56). Morella states in column 21, lines 1-4,

> the mean AUC obtained when the formulations were administered immediately after food were larger than the equivalent value obtained in the fasted state.

Thus, Morella discloses that the bioavailability of his pharmaceutical pellet composition is affected by food intake. To the extent that any of Applicant's earlier statements, including those in the Declaration filed with the Supplemental Amendment of October 24, 2002 could be taken to acknowledge or admit that Morella's formulations exhibit no food effect, Applicant wishes to clarify that a closer reading of Morella supports the position now taken.

Morella provides no guidance for modifying its disclosure to arrive at the subject matter of the amended claims. Morella's concern was to establish that dose dumping (defined in column 1, lines 27-30) was not occurring with either formulation, rather than devising a

formulation that is free of food effect. Morella offers no suggestions as to how to avoid the observed food effect. The tablet composition claimed in amended Claims 1, 9 and 11, on the other hand, is free of food effect as can be seen from table 2 on page 10 of the application.

For these reasons, Applicant respectfully submits that amended claims are patentable under § 103 over the Morella reference. Accordingly, Applicant respectfully requests the rejection be withdrawn.

CONCLUSION

It is believed that all of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider and withdraw all presently outstanding rejections. It is believed that a full and complete response has been made to the outstanding Office Action, and as such, the present application is in condition for allowance. Thus, prompt and favorable consideration of this amendment is respectfully requested. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (248) 641-1600.

Respectfully submitted,

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